

# Primary Cutaneous Lymphoma-Associated Pseudoepitheliomatous Hyperplasia Masquerading as Squamous Cell Carcinoma in a Young Adult

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**Abstract-** Primary cutaneous anaplastic large cell lymphoma is a T-cell malignancy with atypical CD30 positive lymphocytes. Pseudoepitheliomatous hyperplasia is an uncommon finding in primary cutaneous anaplastic large cell lymphoma, and may mimic squamous cell carcinoma as pseudomalignancy. Careful attention of a pathologist to correct diagnosis of pseudoepitheliomatous hyperplasia and its underlying causes will help physicians to avoid inappropriate management. Here, we present a 22-year-old man referred to our hospital with a solitary nodule persistent on his forearm which was diagnosed as squamous cell carcinoma in the first biopsy. The lesion recurred after two months and histopathologic and immunohistochemistry examination revealed anaplastic large cell lymphoma with florid pseudoepitheliomatous hyperplasia which masquerading as well-differentiated squamous cell carcinoma. Diagnosis of pseudoepitheliomatous hyperplasia must guide the pathologist to search for underlying causes, such as primary cutaneous lymphoma. Pseudoepitheliomatous hyperplasia may mimic squamous cell carcinoma and this can result in inappropriate diagnosis and management.

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## Introduction

Primary cutaneous anaplastic large cell lymphoma (ALCL) is a T-cell malignancy and composed of large atypical lymphocytes (1). These cells are anaplastic, pleomorphic or with an immunoblastic cytomorphology and most of them express CD30 antigen (2). Pseudoepitheliomatous hyperplasia (PEH) is present infrequently in primary cutaneous ALCL (3). Pseudoepitheliomatous hyperplasia may mimic squamous cell carcinoma (SCC) and this can result in inappropriate diagnosis and management (4).

## Case Report

A 22-year-old man referred to our hospital with a solitary nodule persistent on his forearm for four months. Incisional biopsy was conducted and histopathologic examination was reported squamous cell carcinoma followed by an excisional biopsy with

proper margins. Squamous cell carcinoma was diagnosed even on excisional biopsy with clear margins (Figure 1A, 1B). After two months, the lesion recurred and the patient referred to our hospital. On physical examination, there was a solitary, firm nodule measuring 1 cm in diameter and re-biopsy was done (unfortunately there is not any photograph from the lesion of the patient). Microscopic examination showed skin tissue with florid PEH and dense infiltration of small mononuclear cells intermixed with scattered large anaplastic cells with pleomorphic nuclei (Figure 2A). The variable amount of eosinophilic cytoplasm with cytoplasmic vacuolation and high mitotic activity is also identified. The first specimen is overviewed and florid PEH has been misinterpreted as well-differentiated SCC. The sparse anaplastic cells within the dermis in the first specimen resulted in inattention and epidermal changes considered as the main pathology (Figure 1B). Pseudoepitheliomatous hyperplasia and dermal infiltration is highlighted by immunoreaction to

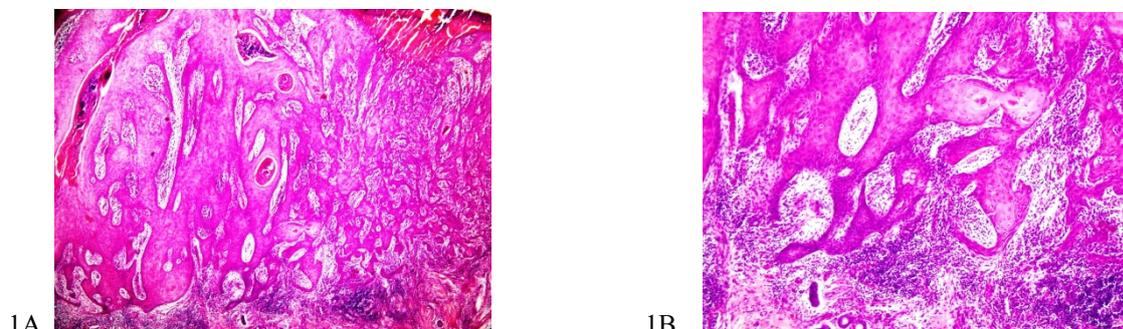
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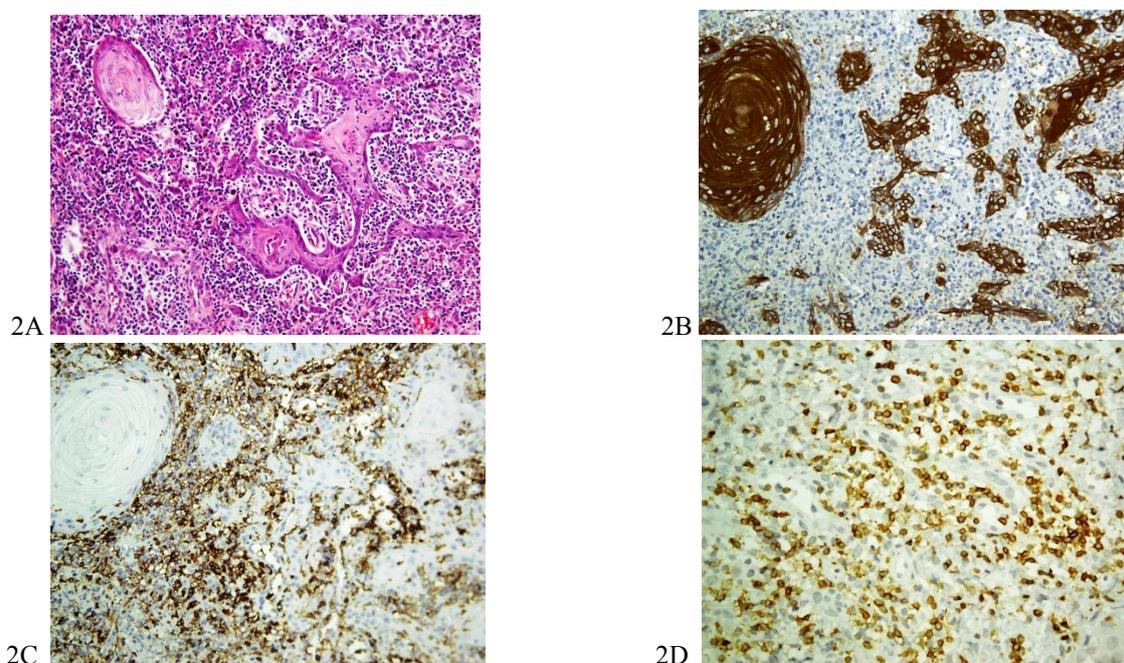
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cytokeratin AE1/AE3 and leukocyte common antigen (LCA), respectively (Figure 2B, 2C). The immunohistochemical staining of the anaplastic large cells within the dermis showed positive reactivity for CD30 (Figure 2D) and negative reaction to ALK

antigen. Furthermore, immunoreaction to CD3 and CD8 is seen in some mononuclear cells. Proliferative marker of Ki67 is positive in 70% to 80% of the tumor cells. These findings confirmed the diagnosis of primary cutaneous ALCL.



**Figure 1.** Pseudoepitheliomatous hyperplasia. A. Marked PEH misinterpreted as SCC in excisional biopsy. (H&E, original magnification×4). B. Higher magnification of the specimen shows interdigitation of squamous nests within underlying infiltration. Note scant infiltration of small mononuclear cells had led to ignore it as main pathology. (H&E, original magnification×10)



**Figure 2.** A. Recurrence of the lesion with severe pseudoepitheliomatous hyperplasia and dense infiltration of mononuclear and pleomorphic cells. (H&E, original magnification×10). B Immunoreaction of PEH with cytokeratin AE1/AE3 (original magnification×20), C. Immunoreaction of dermal infiltration with leukocyte common antigen (LCA) (original magnification×20), D. Immunoreaction of anaplastic large cells with CD30. (original magnification×40)

## Discussion

Primary cutaneous anaplastic large cell lymphoma is a form of cutaneous T-cell lymphoma, which accounts for about 12% of them. It affects adults more

than children and adolescents. Men affected two times more than women. It presents as a localized or solitary papule, nodule or tumor and can develop ulceration. The lesions can undergo partial or complete spontaneous resolution and extracutaneous involvement occurs in about 10% of patients which is

mostly involving regional lymph nodes (2).

The disease is characterized by the presence of large atypical CD30 (Ki-1) positive lymphocytes. Histologically, large anaplastic mononuclear cells with abundant cytoplasm and an eccentric reniform nucleus can be seen. Doughnut cells which have intranuclear cytoplasmic inclusions could be seen occasionally. Two other histopathologic features are lymphohistiocytic variant and small cell variants. Epidermal hyperplasia indicates primary cutaneous ALCL rather than systemic ALCL (1).

Courville *et al.*, in 1999 revealed that epidermal growth factor (EGF), epidermal growth factor receptor (EGFr) and transforming growth factor alpha (TGF alpha) associated with other factors can probably involve in the cutaneous T-cell lymphoma associated epidermal hyperplasia (5). These findings are confirmed in other studies as well. Pseudoepitheliomatous hyperplasia is a benign condition, but it can mimic SCC histopathologically (6). It is characterized by irregular hyperplasia of the epidermis, follicular infundibulum and acrosyringium (7). It never has atypical mitotic figures rather than SCC and dyskeratosis or atypical nuclei are rare (8).

Conditions associated with PEH are classified into four major categories: infections, neoplasia, dermatosis with chronic irritation and inflammation, and miscellaneous process. It is occasionally seen in association with lymphomas such as CD30 lymphoproliferative diseases. It could be of positive prognostic value for spontaneous resolution in some cases of ALCL (6). Histologic distinction between PEH and SCC is often difficult. Consideration and recognition of an underlying cause could be helpful in the diagnosis of PEH. Among underlying causes of PEH, CD30 positive lymphoproliferative disorders are not widely noted in routine pathology literature (9).

Scarisbrick *et al.*, reported three cases of PEH mimicking SCC associated with cutaneous CD30 positive lymphoma in 2001. They concluded PEH associated with CD30 positive lymphoproliferative disease may mimic SCC, and it can cause inappropriate diagnosis and treatment (4). Massone *et al.*, in 2008 reported that pseudoepitheliomatous hyperplasia is one of the rare morphologic findings of primary cutaneous ALCL, and it may lead to misdiagnosis of an epithelial tumor rather than a lymphoproliferative disease (10). Zayour *et al.*, in 2011 reviewed PEH and its underlying causes and proposed a standard approach to PEH interpretation. According to this approach, PEH can be divided into two categories: PEH is the main finding

without dermal changes or the secondary finding of a pathologic process in the dermis (6).

These studies and our case showed that pathologic diagnosis of well-differentiated SCC could be with cautious and if a pathologist encountered in the diagnosis of SCC, he must keep in mind other diagnoses such as PEH. Diagnosis of PEH in histopathology must guide the pathologist to search for underlying causes, such as primary cutaneous lymphoma. Of course, diagnosis of SCC than PEH and its underlying causes may result in inappropriate management of the main disorder.

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